

In the Claims:

Please amend claims 3, 6, 7, and 11, and please add new claims 15-27 as indicated below.

1. (Previously Amended) A method for introducing an intact oligonucleotide into a mammal,
the method comprising the step of orally administering to the mammal a chimeric oligonucleotide, the oligonucleotide comprising about 6 to 50 nucleotides linked via at least one phosphorothioate internucleotide linkage and at least one internucleotide linkage selected from the group consisting of alkylphosphonate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, phosphoramidite, phosphate ester, carbamate, carbonate, phosphate triester, acetamidate, and carboxymethyl ester, the oligonucleotide further comprising at least one 2'-O-alkyl ribonucleotide,

whereby the oligonucleotide is present in intact form in plasma at least six hours following oral administration.

2. (Original) The method of claim 1, wherein the oligonucleotide comprises at least one alkylphosphonate internucleotide linkage.

3. (Currently Amended) The method of claim 2, wherein the oligonucleotide comprises at least one alkylphosphonate internucleotide linkage at its 3' ~~and/or~~ terminal end, at its 5' terminal end, or at its 3' and 5' terminal ends.

4. (Original) The method of claim 3, wherein the oligonucleotide comprises at least two alkylphosphonate internucleotide linkages at its 3' and 5' terminal ends.

5. (Original) The method of claim 2, wherein the oligonucleotide comprises at least one methylphosphonate internucleotide linkage.

6. (Currently Amended) The method of claim 4, wherein the ~~alkyl phosphonate~~alkylphosphonate internucleotide linkage is a methylphosphonate internucleotide linkage.

7. (Currently Amended) The method of claim 1, wherein the oligonucleotide comprises from about ~~from~~ 15 to 25 nucleotides.

8. (Original) The method of claim 1, wherein the oligonucleotide is complementary to a gene of a virus, pathogenic organism, or a cellular gene.

9. (Previously Amended) The method of claim 1, wherein the oligonucleotide is complementary to a gene of a virus involved in a disease selected from the group consisting of AIDS, oral and genital herpes, papilloma warts, influenza, foot and mouth disease, yellow fever, chicken pox, shingles, adult T-cell leukemia, Burkitt's lymphoma, nasopharyngeal carcinoma, and hepatitis.

10. (Previously Amended) The method of claim 1, wherein the oligonucleotide is complementary to a gene encoding a protein associated with Alzheimer's disease.

11. (Currently Amended) The method of claim 1, wherein the oligonucleotide is complementary to a gene encoding a protein in a parasite causing a parasitic disease selected from the group consisting of amebiasis, Chagas' disease, toxoplasmosis, pneumocytosis, giardiasis, cryptosporidiosis, trichomoniasis, malaria, ascariasis, filariasis, trichinosis, schistosomiasis infections.

12. (Cancelled)

13. (Cancelled)

14. (Cancelled)

15. (New) The method of claim 1, wherein the 2'-O-alkyl ribonucleotide is a 2'-O-methyl ribonucleotide.

16. (New) The method of claim 1, wherein the oligonucleotide comprises at least one 2'-O-alkyl ribonucleotide at its 3' terminal end.

17. (New) The method of claim 1, wherein the oligonucleotide comprises at least one 2'-O-alkyl ribonucleotide at its 5' terminal end.

18. (New) The method of claim 1, wherein the oligonucleotide comprises at least one 2'-O-alkyl ribonucleotide at its 3' and 5' terminal ends.

19. (New) The method of claim 18, wherein the oligonucleotide comprises at least two 2'-O-alkyl ribonucleotides at its 3' and 5' terminal ends.

20. (New) The method of claim 15, 16, 17, or 18, wherein the 2'-O-alkyl ribonucleotide is a 2'-O-methyl ribonucleotide.

21. (New) The method of claim 15, 16, 17, or 18, wherein the 2'-O-alkyl ribonucleotide is further substituted.

22. (New) The method of claim 21, wherein the 2'-O-alkyl ribonucleotide is further substituted with a substituent selected from the group consisting of halo, hydroxyl, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl and amino groups.

23. (New) A method for introducing an intact oligonucleotide into a mammal, the method comprising the step of orally administering to the mammal a chimeric oligonucleotide, wherein the oligonucleotide comprises 15 to 25 nucleotides linked via at least one phosphorothioate internucleotide linkage,

wherein the oligonucleotide further comprises at least two alkylphosphonate internucleotide linkages at its 3' and 5' terminal ends,

wherein the oligonucleotide further comprises at least two 2'-O-alkyl ribonucleotides at its 3' and 5' terminal ends, and wherein the oligonucleotide is present in intact form in plasma at least six hours following oral administration.

24. (New) The method of claim 23, wherein the alkylphosphonate internucleotide linkages flank a section of the oligonucleotide comprising at least two phosphorothioate internucleotide linkages.

25. (New) The method of claim 23 or 24, wherein the two 2'-O-alkyl ribonucleotides are 2'-O-methyl ribonucleotides.

26. (New) The method of claim 23 or 24, wherein the 2'-O-alkyl ribonucleotides are further substituted.

27. (New) The method of claim 26, wherein the 2'-O-alkyl ribonucleotide is further substituted with a substituent selected from the group consisting of halo, hydroxyl, trifluoromethyl, cyano, nitro, acyl, acyloxy, alkoxy, carboxyl, carbalkoxyl and amino groups.
